

Fig. 1

00000000000000000000000000000000

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Fig. 2A

□ □ □ □ □ □ □ □ □ □

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Fig. 2B (sheet 1 of 3)

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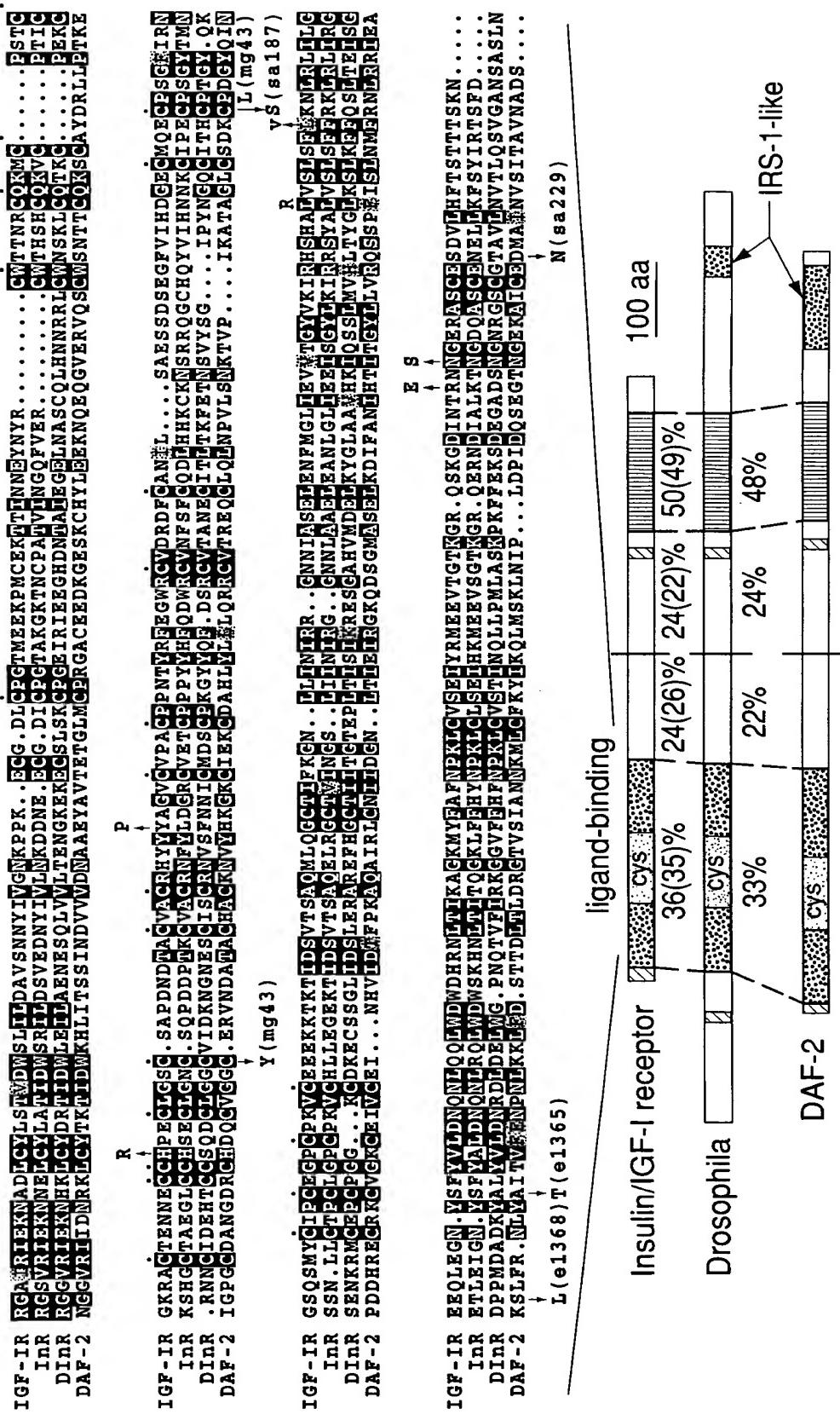
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Fig. 2B (sheet 2 of 3)

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Fig. 2B (sheet 3 of 3)

Fig. 2C (sheet 1 of 2)



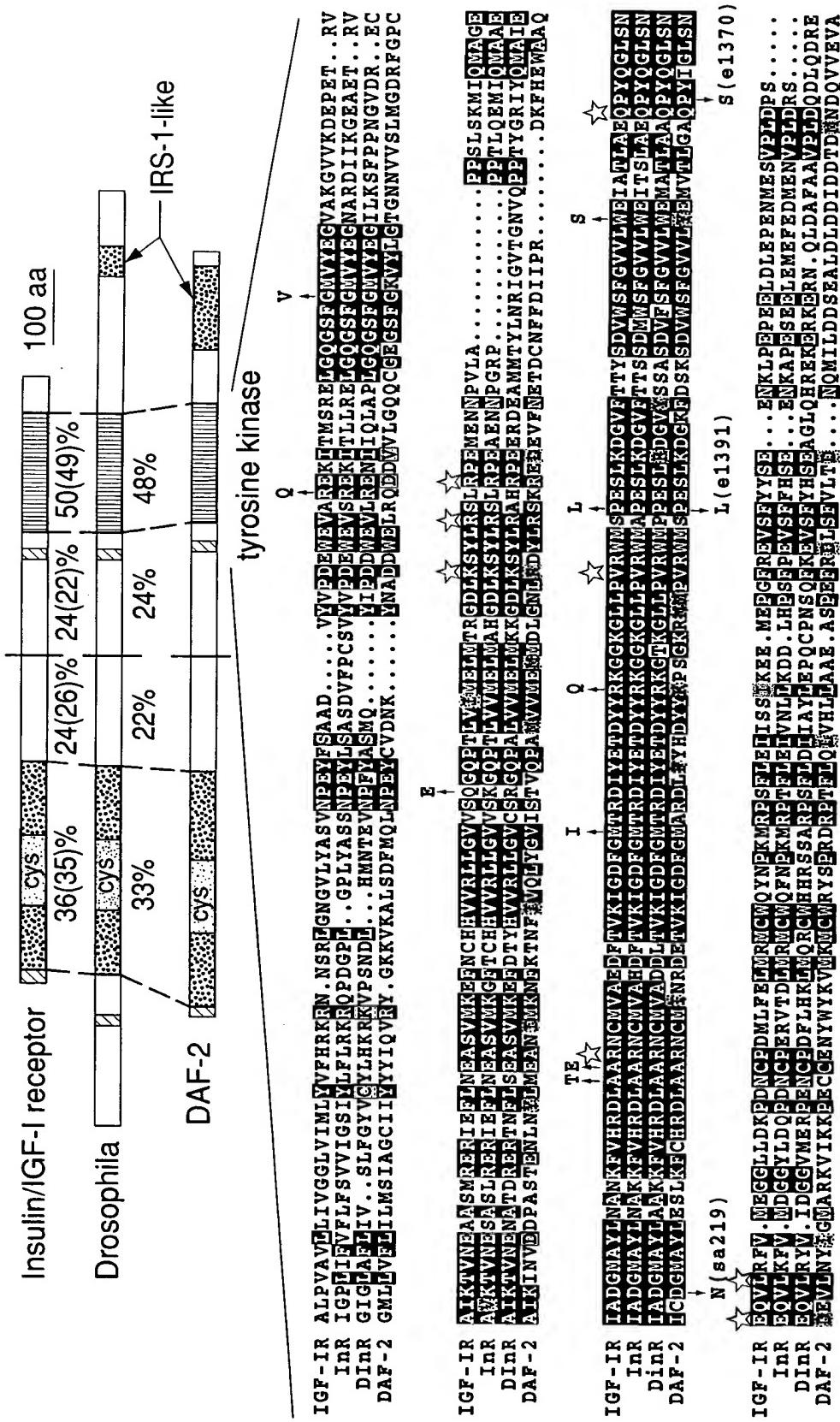


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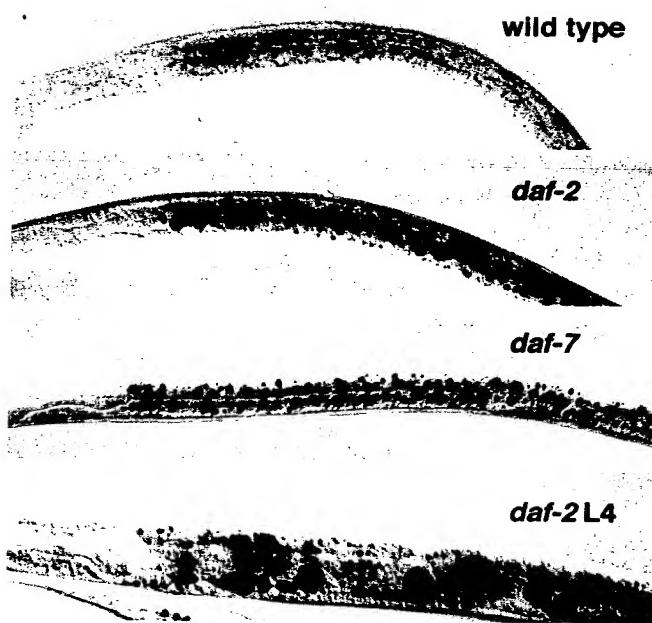


Fig. 3

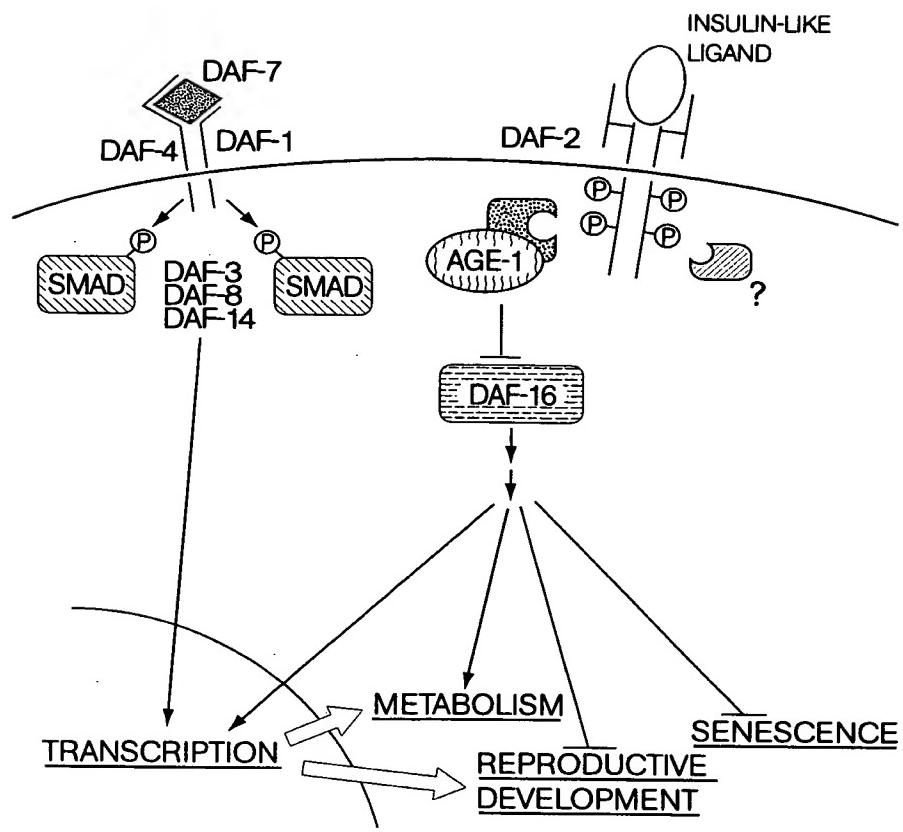


Fig. 4

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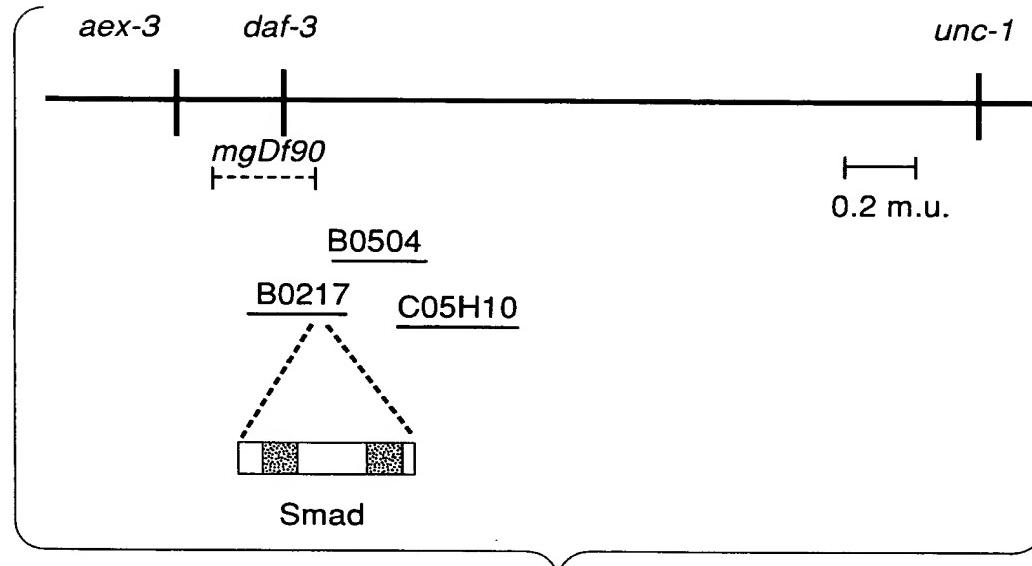


Fig. 5A

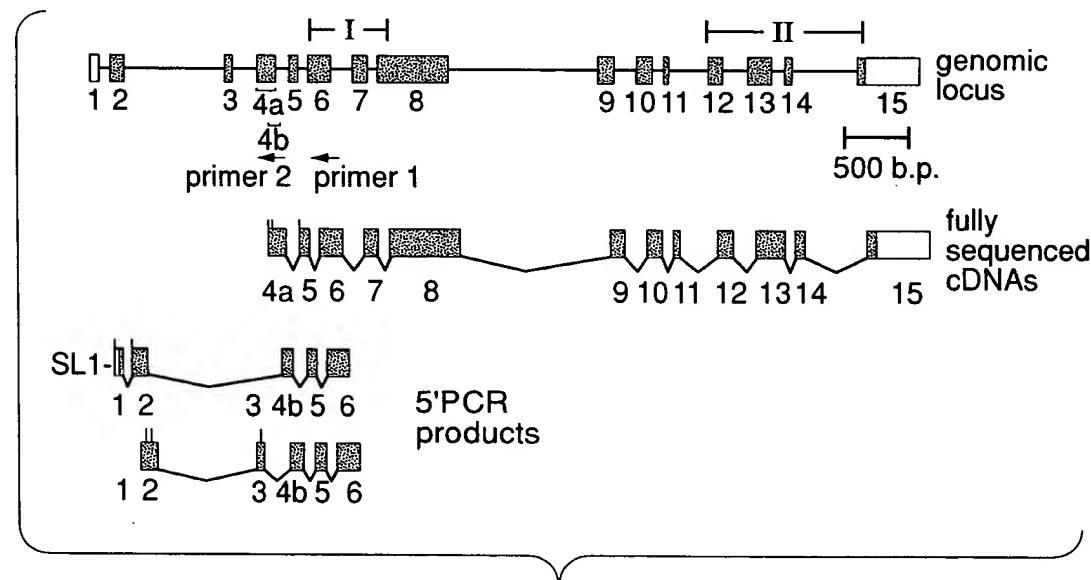


Fig. 5B

263452052025

Domain I

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	<i>mg125 P->L</i>
	RLQVHGRKGFPVYVYGKLWRFNEMTKNETRHVDHCKHAFEMKSDMVCVNPHYH
	RLQVAGRKGFPVHVIYARLWRWPDLHKNELKHVKYCQYAFDLKCDSCVNPYH

Domain II

DAF-3	IVYYEKNLQIGE..KKCSRGNFHVDGGFI..CSENRYSLGLEPNPIREPVAFKV
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	<i>mg132 G->E</i>
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Fig. 5C

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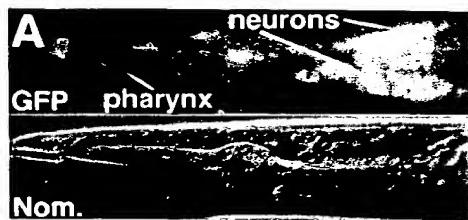


Fig. 6A

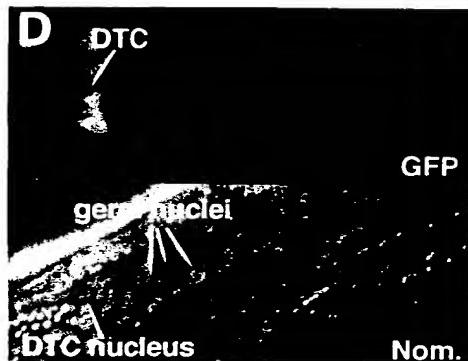


Fig. 6D

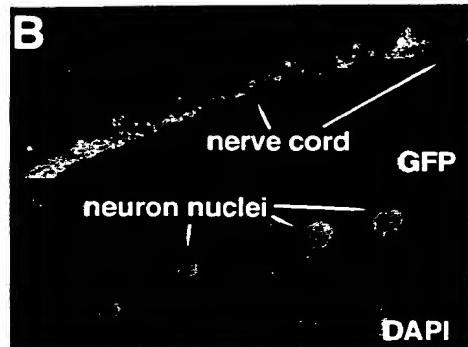


Fig. 6B

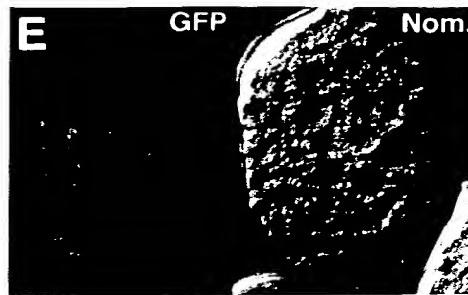


Fig. 6E

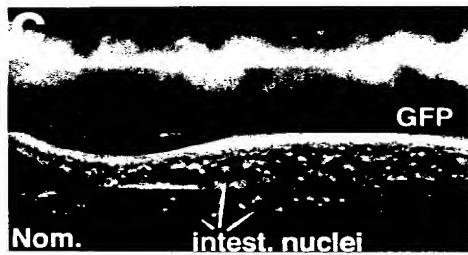


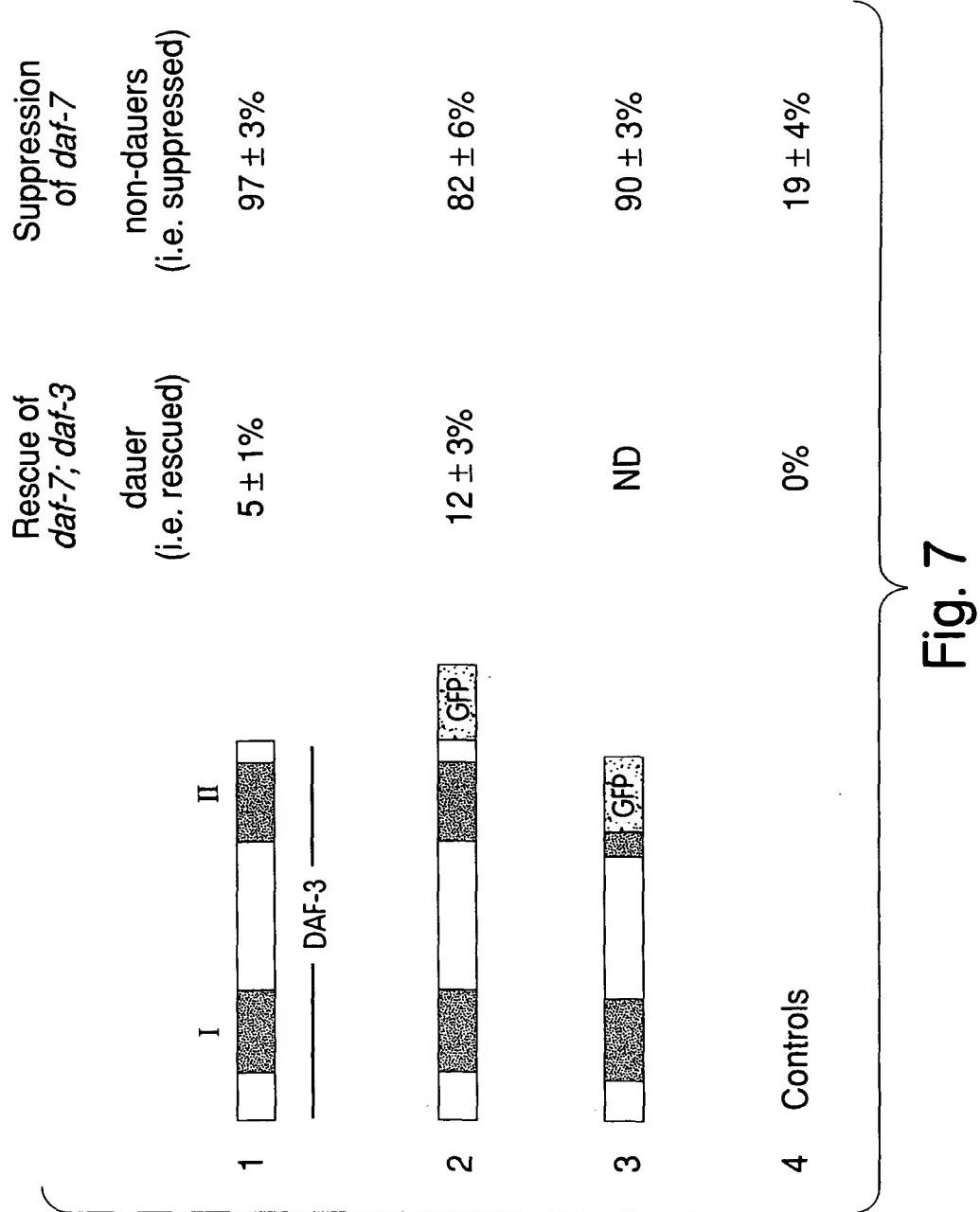
Fig. 6C



Fig. 6F



Fig. 6G



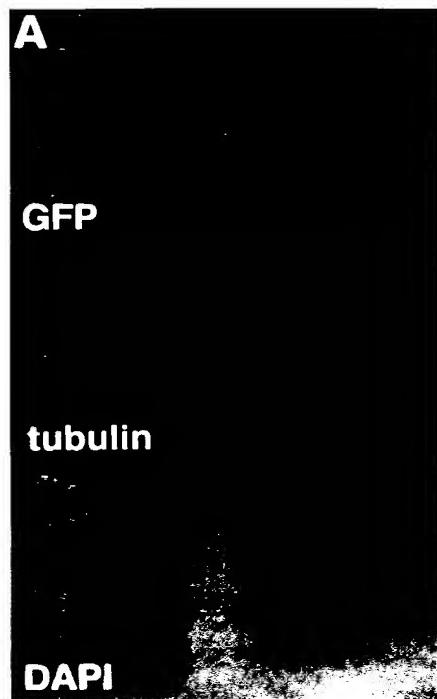


Fig. 8A

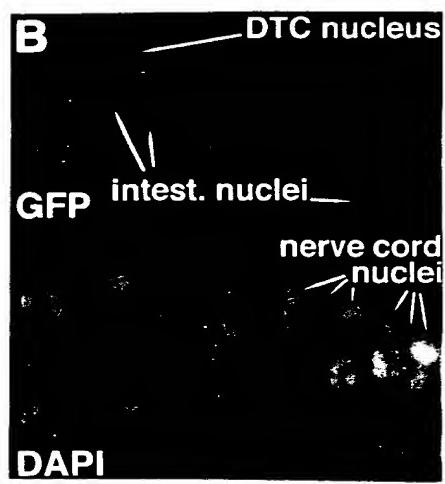


Fig. 8B

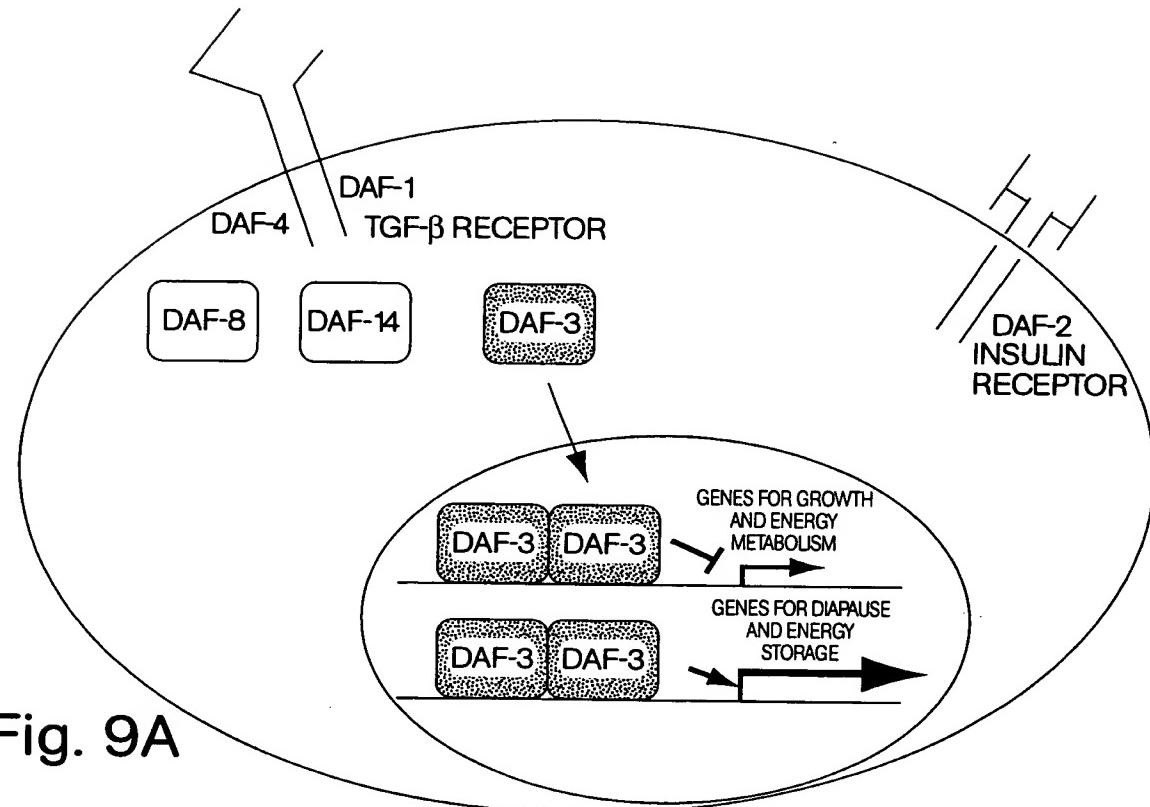


Fig. 9A

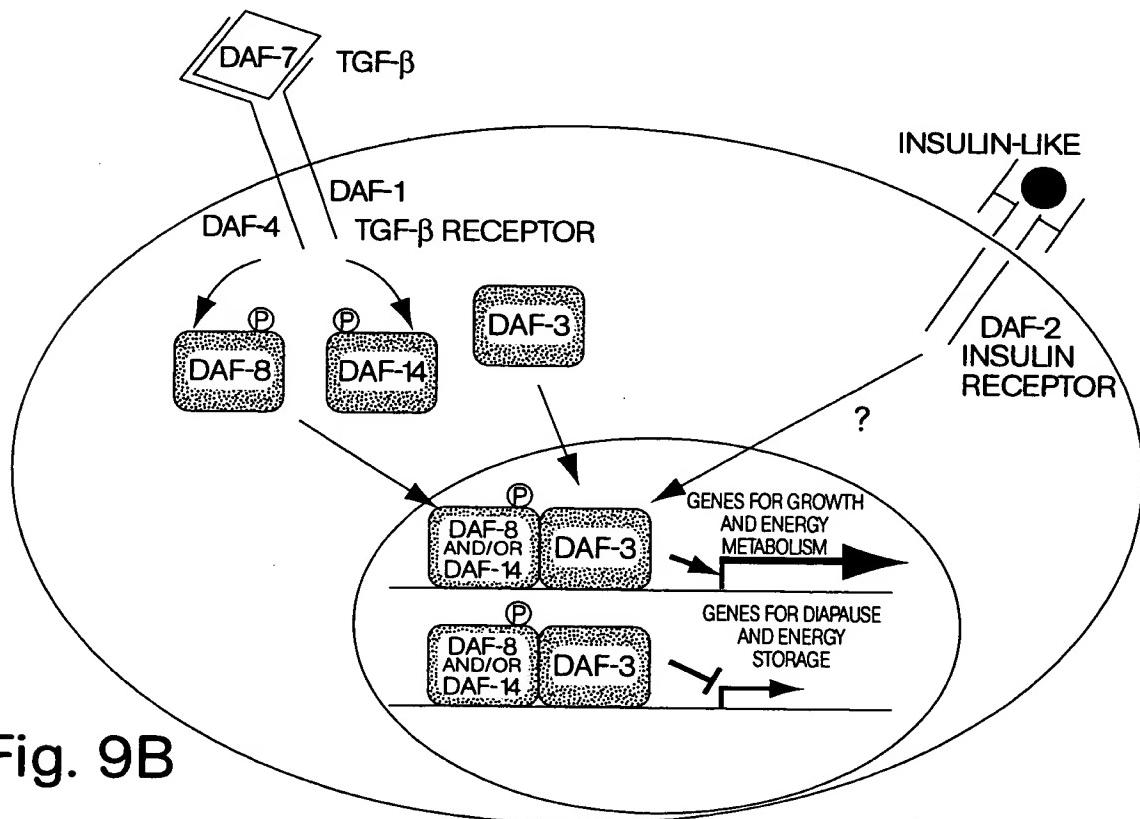


Fig. 9B

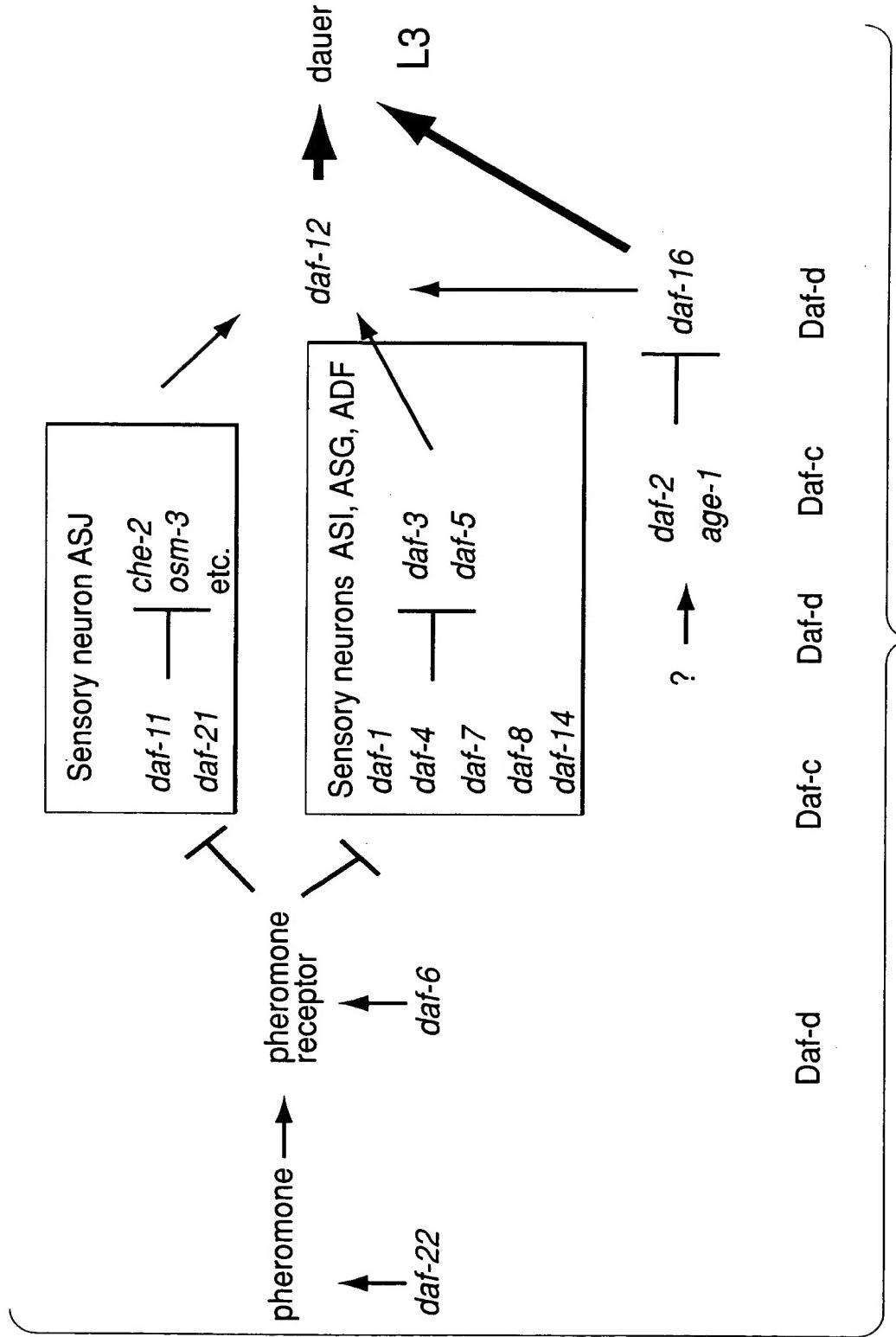


Fig. 10

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1901 aaaaccgcattt gaaatccccg gtatttgca cttctggta tctcgacgag
1951 caatcaggag gcctaaagaa ggataaaagtgc cacaatgtt acggatgtgc
2001 gtctatcaaa acgtttggct tcaacgtttc caaacaatc atcagagacg
2051 cgcttcttc caagcaaatg gcaacaatgt acttgcaagg aaaattgact

Fig. 11A (sheet 1 of 2)

2101 ccgatgaatt atatctacga gaagaagact caggaagagc tgcgaaggaa
2151 agcaacacgc accactgatt cattggccaa gtactgttgt gtccgtgtct
2201 cggtctgcaa aggatttggga gaagcatacc cagaacgccc gtcaattcat
2251 gattgtccag tttggattga gttgaaaatc aacattgcct acgatttcat
2301 ggattcaatc tgccagtaca taaccaactg cttcgagccg ctaggaatgg
2351 aagattttgc aaaattggga atcaacgtca gtgatgacta aatgataact
2401 ttttcactc accctactag atactgattt agtcttattc caaatcatcc
2451 aacgatataca aacttttcc tttgaacttt gcataactatg ttatcacaag
2501 ttccaaggcag tttcaataca aacataggat atgttaacaa cttttgataaa
2551 gaatcaagtt accaactgtt cattgtgagc tttgagctgt atagaaggac
2601 aatgttatccc atacctcaat cttaatagt catcagtcac tggccccgca
2651 ccaattttt cgattcgcat atgtcatata ttgcaccgtg gccctttta
2701 ttgttaacttt taatatattt tcttcccaac ttgtgaatat gattgatgaa
2751 ccaccatttt gagtaataaa tgtatTTT gtgg

Fig. 11A (sheet 2 of 2)

1 gtaatcaa at tgtaaaggaa aaatattaat agtcagagta cacataaatg
51 ggtgatcatc ataatttaac gggccttccc ggtacccca tccccccaca
101 gttcaactat tctcagcccg gtaccagcac cggaggccccg ctttatggtg
151 gaaaaccttc tcattggattt gaagatattt ctgtatgtaga ggaatatgag
201 aggaacctgc tcggggctgg agcaggttt aatctgctca atgttagaaaa
251 tatggcta at gttcccgacg agcacacacc gatgtatgtca ccagtgaata
301 caactacaaa gattctacaa cggagtggta ttaaaatgga aatcccgcca
351 tatttggatc cagacagtca ggatgtatgc ccggaagatg gtgtcaacta
401 cccggatcca gatttattt acacaaaaaa cacaatatg accgagtagc
451 atttggatgt gttgaagctt ggaaaaccag cagtagatga agcacgaaaa
501 aagatcgaag ttcccacgc tagtgcgcg ccaaacaaaa ttgtagaata
551 tttgatgtat tatagaacgt taaaagaaag tgaactcata caactgaatg
601 cgtatcgac aaaacgaaat cgattatcg tgaacttggc caaaaacaat
651 attgatcgag agttcgacca aaaagcttc gagtccctgg tgaaaaaatt
701 gaaggataag aagaatgatc tccagaacct gattgtatgt gttcttcaa
751 aaggtacaaa atataccggt tgcattacaa ttccaaggac acttgatggc
801 cggttacagg tccacggaa gaaaggttc cctcacgtag tctatggcaa
851 actgtggagg tttaatgaaa tgacaaaaaa cgaacgcgt catgtggacc
901 actgcaagca cgcatggaa atgaaaagtg acatggatg cgtgaatccc
951 tatcactacg aaattgtcat tggaactatg attgttggc agagggatca
1001 tgacaatcga gatatgccgc cgccacatca acgctaccac actccaggc
1051 ggcaggatcc agttgacgat atgagtagat ttataccacc agcttccatt
1101 cgtccgcctc cgatgaacat gcacacaagg cctcagccta tgcctcaaca
1151 attgccttca gttggcgaa cgtttgcctt tcctctccca catcaggcgc
1201 cacataaccc aggggttca catccgtact ccattgctcc acagaccat
1251 tacccgttga acatgaaccc aattccgaa atgcccggaa tgccacaaat
1301 gccaccaccc ctccatcagg gatatggaat gaatggccg agttgctt
1351 cagaaaacaa caatccattc caccaaaatc accattataa tgatattagc
1401 catccaaatc actattccta cgactgttgtt ccgaacttgt acgggttcc
1451 aactccttat ccggattttc accatcctt caatcagcaa ccacaccagc
1501 cgccacaact atcacaaaac catacgtccc aacaaggcag tcatcaacca
1551 gggcaccaag gtcaggtacc gaatgtatca ccaatttcaa gaccagtgtt
1601 acaaccatca acagtcaccc tggacgttgtt ccgtcggtac tgtagacaga
1651 cattggaaa tcgatttttt gaaggagaaa gtacaatc cggcgcaata
1701 attcggtcta gtaacaaatt cattgaagaa tttgattcgc cgatttgtgg
1751 tgtgacagtt gttcgaccgc ggatgacaga cggtgagggtt ttggagaaca
1801 tcatgccgga agatgcacca tatcatgaca tttgcaagtt cattttgagg
1851 ctcacatcag aaagtgtaac tttctcaggaa gagggccag aagttagtga
1901 ttgtgacgaa aaatggggaa caattgtgtt ctatgagaaa aatttgcaaa
1951 ttggcgagaa aaaatgttcg agagggaaatt tccacgttgcg tggcgattc
2001 atttgctctg agaatcgatc cagtcgttgc cttgagccaa atccaattag
2051 agaaccagtg gcgtttaaag ttcgttgc aatagtgat ggaattcgct

Fig. 11B (sheet 1 of 2)

2101 tttcctacaa aaaagacggg agtgttggc ttcaaaaccg catgaagtac
2151 ccggatttg tcacttctgg gtatctcgac gagcaatcg gaggcctaaa
2201 gaaggataaa gtgcacaaag tttacggatg tgcgtctatc aaaacgtttg
2251 gcttcaacgt ttccaaacaa atcatcagag acgcgcttct ttccaagcaa
2301 atggcaacaa tgtacttgca aggaaaattt actccgatga attatatcta
2351 cgagaagaag actcaggaag agctgcgaag ggaagcaaca cgcaccactg
2401 attcattgac caagtactgt tgtgtccgtg tctcggtctg caaaggattt
2451 ggagaagcat acccagaacg cccgtcaatt catgattgtc cagtttggat
2501 tgagttgaaa atcaacattt cctacgattt catggattca atctgccagt
2551 acataaccaa ctgcttcgag ccgcgttagaa tggaagattt tgcaaaattt
2601 ggaatcaacg tcagtgtatca ctaaatgata actttttca ctcaccctac
2651 tagatactga ttttagtctta ttccaaatca tccaaacgata tcaaactttt
2701 tcctttgaac tttgcataact atgttatcac aagttccaag cagttcaat
2751 acaaacatag gatatgttaa caactttga taagaatcaa gttaccaact
2801 gttcattgtg agcttgagc tgtatagaag gacaatgtat cccataacctc
2851 aatcttaat agtcatcagt cactggccc gcaccaattt ttgcattcg
2901 catatgtcat atattgcacc gtggccctt ttattgtaac tttaatata
2951 tttcttccc aacctgtgaa tatgattgat gaaccaccat ttgagtaat
3001 aaatgttattt ttgtgg

Fig. 11B (sheet 2 of 2)

1 gtaatcaa at taaaaaggaa aaatatta at agtcagagta cacataa atg
 51 ggtgatcatc ataatttaac gggccttccc ggtacctcca tccccccaca
 101 gttcaactat tctcagcccg gtaccagcac cggaggcccg cttagtg
 151 gaaaaccttc tcattggattt gaagatattt ctgtatgtaga ggaatatgag
 201 agaacctgc tcggggctgg agcagggttt aatctgctca atgttaggaaa
 251 tatggctaat gaatttaaac caataatcac attggacacg aaaccacctc
 301 gtatgc ccaa caagtcatgg gcattcaatg gcgggtt gaa gcta atcact
 351 ccgaaaactg aagttcccga cgagcacaca ccgatgatgt caccagt gaa
 401 tacaactaca aagattctac aacggagtgg tattaaaatg gaaatcccgc
 451 catattt gga tccagacagt caggatgatg acccggaa gttgtcaac
 501 tacccggatc cagatttatt tgacacaaaa aacacaaata tgaccgagta
 551 cgatttggat gtgttgaagc ttggaaaacc agcagtagat gaagcacgga
 601 aaaagatcga agtccc gac gctagtgcgc cgccaaacaa aattttagaa
 651 tattt gatgtt attatagaac gttaaaagaa agtgaactca tacaactgaa
 701 tgcgtatcg acaaaacgaa atcgattt atcgattt gttgaactt gtc
 751 atattt gatcg agat tgcac caaaaagctt gcgagtcctt ggtgaaaa
 801 ttgaaggata agaagaatga tctccagaac ctgattgatg tggttctt
 851 aaaaggta aatataccg gttcattt aatttcaagg acacttgatg
 901 gccgg taca ggtccacgg agaaaagg tccctcacgt agtctatggc
 951 aaactgtgga ggtttaatga aatgacaaaa aacgaaacgc gtc
 1001 ccaactgcaag cacgcattt aatgaaaag tgacatggta tgcgtgaaatc
 1051 cctatcacta cgaaattgtc attgaaacta tgattt gtc
 1101 catgacaatc gagatatgcc gcccacat caacgctacc acactccagg
 1151 tcggcaggat ccagttgacg atatgatgatg atttatacca ccagcttcca
 1201 ttgcgtccgccc tccgatgaaatgc acacacaa ggc
 1251 caattgcctt cagttggcgc aacg tttgccc catcctctcc
 1301 gccacataac ccagggtt cacatccgta ctccattgct
 1351 attaccggtt gaacatgaa ccaattccgc aatgccc
 1401 atgccc accac ctctccatca gggatatgga atgaatggc
 1451 ttca gaaaac aacaatccat tccaccaaaa tcaccattat
 1501 gccatccaaa tcactattcc tacgactgtg gtcc
 1551 ccaactcctt atccggattt tcaccatcct tcaatcagc
 1601 gccc
 1651 cagggcacca aggtcaggta ccgaatgatc
 1701 ttacaaccat caacagtac cttggacgtg
 1751 gacattt gga aatcgattt ttgaaggaga aagtgaacaa
 1801 taattcggtc tagtacaaa ttcatgaa
 1851 ggtgtgacag ttgttcgacc gcggatgaca
 1901 catcatgccc
 1951 ggctcacatc agaaatgtt
 2001 gattt gaa
 2051 gatggc
 2101 gggccatgtt
 2151 gatggccatgtt
 2201 gatggccatgtt
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2101 tcatttgctc tgagaatcg tacagtctcg gacttgagcc aaatccaatt
2151 agagaaccag tggcgttaa agttcgtaaa gcaatagtgg atggaattcg
2201 ctttcctac aaaaaagacg ggagtgttg gcttcaaaac cgcatgaagt
2251 acccggtatt tgtcacttct gggtatctcg acgagcaatc aggaggccta
2301 aagaaggata aagtgcacaa agttacgga tgtgcgtcta tcaaaacgtt
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2701 tggaaatcaa cgtcagtgtat gactaaatga taacttttt cactcaccct
2751 actagatact gatttagtct tattccaaat catccaaacga tatcaaactt
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2851 atacaaacat aggatatgtt aacaactttt gataagaatc aagttaccaa
2901 ctgttcattt tgagcttta gctgtataga aggacaatgt atcccatacc
2951 tcaatcttta atagtcata gtcactggtc ccgcaccaat ttttcgatt
3001 cgcataatgtc atatattgca ccgtggccct ttttattgtt aacttttaata
3051 tattttcttc ccaacttgtt aatatgattt atgaaccacc attttgagta
3101 ataaaatgtat tttttgtgg

Fig. 11C (sheet 2 of 2)

1	MKLIATSLLV	PDEHTPMMSP	VNTTTKILQR	SGIKMEIPPY	LDPDSQDDDP
51	EDGVNYPDPD	LFDTKNTNMT	EYDLDVLKLG	KPAVDEARKK	IEVPDASAPP
101	NKIVEYLMYY	RTLKESELIQ	LNAYRTKRN	LSLNLVKNNI	DREFDQKACE
151	SLVKKLKDKK	NDLQLNIDVV	LSKGTKYTGC	ITIPRTLDGR	LQVHGRKGFP
201	HVVYGKLWRF	NEMTKNETRH	VDHCKHAFEM	KSDMVCVNPy	HYEIVIGTMI
251	VGQRDHNRD	MPPP HQRYHT	PGRQDPVDDM	SRFIPPASIR	PPPMNMHTRP
301	QPMPQQQLPSV	GATFAHPLPH	QAPHNPVGSH	PYSIAPQTHY	PLNMNPIPQM
351	PQMPQMPPL	HQGYGMNGPS	CSSENNNPFH	QNHHYNDISH	PNHYSYDCGP
401	NLYGFPTPYP	DFHHPFNQQP	HQPPQLSQNH	TSQQGSHQPG	HQGQVPNDPP
451	ISRPVLQPST	VTLDVFRRYC	RQTFGNRFFE	GESEQSGAII	RSSNKFIEEF
501	DSPICGVTVV	RPRMTDGEVL	ENIMPEDAPY	HDICKFILRL	TSESVTFSGE
551	GPEVSDLNEK	WTIVYYEKN	LQIGEKCSR	GNFHVDGGFI	CSENRYSLGL
601	EPNPIREPVA	FKVRKAIVDG	IRFSYKKDGS	VWLQNRMKYP	VFVTSGYLDE
651	QSGGLKKDKV	HKVYGCASIK	TFGFNVSKQI	IRDALLSKQM	ATMYLQGKLT
701	PMNYIYEKKT	QEELRREATR	TTDSLAKYCC	VRVSFCKGFG	EAYPERPSIH
751	DCPVWIELKI	NIAYDFMDSI	CQYITNCFEP	LGMEDFAKLG	INVSD

Fig. 12A

1 MGDHHNLTGL PGTSIPPQFN YSQPGTSTGG PLYGGKPSHG LEDIPDVEEY
51 ERNLLGAGAG FNLLNVGNMA NVPDEHTPMN SPVNTTTKIL QRSGIKMEIP
101 PYLDPDSQDD DPEDGVNYPD PDLFDTKNTN MTEYDLDVLK LGKPAVDEAR
151 KKIEVPDASA PPNKIVEYLM YYRTLKESEL IQLNAYRTKR NRLSLNLVKN
201 NIDREFDQKA CESLVKKLKD KKNDLQNLID VVLSKGTKYT GCITIPRTLD
251 GRLQVHGRKG FPHVVYGKLW RFNEMTKNET RHVDHCKHAF EMKSDMVCVN
301 PYHYEIVIGT MIVGQRDHDN RDMPPPHQRY HTPGRQDPVD DMSRFIPPAS
351 IRPPPMNMHT RPQPMPQQLP SVGATFAHPL PHQAPHNPVG SHPYSIAPQT
401 HYPLNMNPIP QMPQMPQMPP PLHQGYGMNG PSCSSENNNP FHQNHHYNDI
451 SHPNHYSYDC GPNLYGFPTP YPDFHHPFNQ QPHQPPQLSQ NHTSQQGSHQ
501 PGHQGQVPND PPISRPVLPQ STVTLDVFRR YCRQTFGNRF FEGESEQSGA
551 IIRSSNKFIE EFDSPICGVT VVRPRMTDGE VLENIMPEDA PYHDICKFIL
601 RLTSESVTFS GEGPEVSDLN EKWGTIVYYE KNLQIGEKKC SRGNFHVDGG
651 FICSENRYSL GLEPNPIREP VAFKVRKAIV DGIRFSYKKD GSVWLQNRMK
701 YPVFVTSGYL DEQSGGLKKD KVHKVYGCAS IKTFGFNVSK QIIRDALLSK
751 QMATMYLQGK LTPMNYIYEK KTQEELRREA TRTTDSLAKY CCVRVSFCKG
801 FGEAYPERPS IHDCPVWIEL KINIAYDFMD SICQYITNCF EPLGMEDFAK
851 LGINVSD

Fig. 12B

1	MGDHNLNTGL	PGTSIPPQFN	YSQPGTSTGG	PLYGGKPSHG	LEDIPDVEEY
51	ERNLLGAGAG	FNLLNVGNMA	NEFKPIITLD	TKPPRDANKS	LAFNGGLKLI
101	TPKTEVPDEH	TPMMSPVNNT	TKILQRSGIK	MEIIPPYLDPD	SQDDDPEDGV
151	NYPDPDLFDT	KNTNMTEYDL	DVLKLGKPAV	DEARKKIEVP	DASAPPNKIV
201	EYLMYYRTLK	ESELIQLNAY	RTKRNRLSLN	LVKNNIDREF	DQKACESLVK
251	KLKDCKNDLQ	NLIDVVLSKG	TKYTGCITIP	RTLDGRLQVH	GRKGFPVVY
301	GKLWRFNEMT	KNETRHVDHC	KHAFEMKSDM	VCVNPYHYEI	VIGTMIVGQR
351	DHDNRDMPFP	HQRYHTPGRQ	DPVDDMSRFI	PPASIRPPPM	NMHTRPQPMP
401	QQLPSVGATF	AHPLPHQAPH	NPGVSHPYSI	APQTHYPLNM	NPIPQMPPQMP
451	QMPPPPLHQGY	GMNGPSCSSE	NNNPFHQNH	YNDISHPNHY	SYDCGPNLYG
501	FPTPYPDFHH	PFNQQPHQPP	QLSQNHTSQQ	GSHQPGHQGQ	VPNDPPISRP
551	VLQPSTVTLD	VFRYYCRQTF	GNRFFEGERE	QSGAIIRSSN	KFIEFDSP
601	CGVTVVRPRM	TDGEVLENIM	PEDAPYHDIC	KFILRLTSES	VTFSGEGPEV
651	SDLNEKWGTI	VYYEKNLQIG	EKKCSRGNFH	VDGGFICSEN	RYSLGLEPNP
701	IREPVAFKVR	KAIVDGIRFS	YKKDGSVWLQ	NRMKYPVFVT	SGYLDEQSGG
751	LKKDKVHKVY	GCASIKTFGF	NVSKQIIRDA	LLSKQMATMY	LQGKLTPMNY
801	IYEKKTQEEL	RREATRTTDS	LAKYCCVRVS	FCKGFGEAYPE	ERPSIHDCPV
851	WIELKINIA	DFMDSCIQYI	TNCFEPLGME	DFAKLGINV	DD

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Fig. 12C

Fig. 13A

0 1 2 3 4 5 6 7 8 9

ttacacgtggccaatgcaacaatacatctatcaggaatcgtagcaaccattccccataccattaaatcaacacaaca
atccgttatcatccaatgcacccatcatcaattacctcatatgcacaacttcctcaaccttattgaatcttaacatg
acgacgttaacatcttctggcagttccgtggccagttccattggaggcggagctcaatgctccgtgcgcgtcgggctc
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aagccaaaccgatcaattggcacagaagaaccgaatccatgggtgaggaatcttattcgatattgccttgcggatcatt
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Fig. 13B

TOP SECRET - EDITION 2

MMEMLVDQGTDASSASTSTSSVSRFGADTFMNTPDDVMMNDMEPIPRDR
CNTWPMRRPQLEPPLNSSPIIHEQIPEEDADLYGSNEQCGQLGGASSNGST
AMLHTPDGSNSHQTSFPSDFRMSESPDDTVSGKTTTRRNAWGNMSYAELI
TTAIMASPEKRRTLQAQVYEWMVQNVPYFRDKGDSNSSAGWKNSIRHNLSLH
SRFMRIQNEGAGKSSWWVINPDAKPGMNPRRTRERSNTIETTTKAQLEKSR
RGAKKRIKERALMGLHSTLNGNSIAGSIQTISHDLYDDDSMQGAFDNVPS
SFRPRTQSNL SIPGSSSRVSPAIGSDIYDDLEFPSWVGESVPAIPSDIVDR
TDQMRIDATTHIGGVQIKQESKPIKTEPIAPPSYHELNSVRGSCAQNPLL
RNPIVPSTNFKPMLPGAYGNYQNGGITPINWLSTSNSPLPGIQSCGIVAA
AQHTVASSSALPIDLENLTLPDQPLMDTMDVDALIRHELSQAGGQHIHFDL

Fig. 14A

MQQYIYQESSATIPHHLNQHNNPYHPMHPHHQLPHMQQLPQPLLNLNMTT
LTSSGSSVASSIGGAQCSPCASGSSTAATNSSQQQQTVGQMLAASVPCSS
SGMTLGMSLNLSQGGGPMPAKKKRCKPTDQLAQKKPNPWGEESYSIIIA
KALE SAPDGRLKLNEIYQWFSDNIPYFGERSSPEEAAGWKNSIRHNLSLHS
RFMRIQNEGAGKSSWWVINPDAKPGMNPRRTRERSNTIETTTKAQLEKSRR
GAKKRIKERALMGLHSTLNGNSIAGSIQTISHDLYDDDSMQGAFDNVPS
FRPRTQSNL SIPGSSSRVSPAIGSDIYDDLEFPSWVGESVPAIPSDIVDRT
DQMRIDATTHIGGVQIKQESKPIKTEPIAPPSYHELNSVRGSCAQNPLL
RNPIVPSTNFKPMLPGAYGNYQNGGITPINWLSTSNSPLPGIQSCGIVAA
QHTVASSSALPIDLENLTLPDQPLMDTMDVDALIRHELSQAGGQHIHFDL

Fig. 14B

0 1 2 3 4 5 6 7 8 9

1 cggaagccat ggagctcgag atctgattgc tggacacgga cggaactccg acgttatctcg
61 cagatgcatg ttaacatttt acatccacaa ctgcaaacga tggtcgagca gtggcaaatg
121 cgagaacgcc catcgcttga gaccgagaat ggcaaaggat cgctgctcct gaaaatgaa
181 ggtgtcgag atatcatcac tatgtgtcca ttccggagaag ttattagtgt agtatttccg
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361 gtgttcagac agttgaataa ttccggcgaa attgaagttt tatttaacga cgatcaaccc
421 ctgtcgaaat tagagctcca cggcactttc ccaatgctt ttctctacca acctgatgga
481 ataaacacaggg ataaagaatt aatgagtgtat ataagtctt gtctaggata ctcactggat
541 aaacttggaaag agagcctcg a ttaggaactc cgtcaatttc gtgttctct ctgggctcg
601 acgaagaaaa cgtgcttgc acgtggactt gagggtacca gtcactacgc gtccccgaa
661 gaacagtact tttgtgttgg tgaatcgtgc ccgaaagatt tggaaatcaa agtcaaggct
721 gccaagctga gttatcagat gttttggaga aaacgtaaag cgaaatcaa tggagtttgc
781 gagaaaaatga tgaagatca aattgaattt aatccgaacg aaactccgaa atctctgctt
841 cacacgtttc tctacgaaat gcgaaaattt gatgtatacg ataccgatga tcctgcagat
901 gaaggatggt ttcttcaatt ggctggacgt accacgtttt ttacaatcc agatgtcaaa
961 cttacgtctt atgatgggtt ccgttcggaa ctggaaagct atcgatgccc tgattcggt
1021 gttccggac aatcactagt cctcaaagac tattgtcgcc caaaaccact ctacgaacca
1081 cattatgtga gggcacacga acgaaaactt gctctagacg tgctcagcgt gtctatagat
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2221 tggctgctcc gtgcagagat tgctcgatgg agagattgtt atctgaaaag tgaagaatat
2281 cggcgatct cacttctgtat ggaagcttac ctccgtggaa atgaagagca catcaagatc
2341 atcaccggac aagttgacat ggttgtatgg ctcacacgaa tcagcactt tttgttggaa
2401 atgccaaaag atggtgttgc gatgaaactg cgtgacgagc ttgcgtatgt tagtcataaa
2461 atggaaaata tggattctcc actggatcct gtgtacaaac tgggtgaaat gataatcgac
2521 aaagccatcg tccttaggaag tgcacacgt ccgttaatgc ttcaactggaa gaacaaaaat
2581 ccaaagagtg acctgcaccc tccgttctgt gcaatgatct tcaagaatgg agacgatctt
2641 cgccaggaca tgcttcttgc tcaagttctc gaagttatgg ataacatctg gaaggctgca

Fig. 15 (sheet 1 of 2)

2701 aacattgatt gctgttgaa cccgtacgca gttctccaa tggagaaaat gattgaaatt
2761 attgaagttg tgcctaattt taaaacaata ttcgagattc aagttggAAC aggattcatg
2821 aatacagcag ttccggatgtat tgatccttcg tttatgaata agtggattcg gaaacaatgc
2881 ggaattgaag atgaaaagaa gaaaagcaaa aaggactcta cgaaaaatcc catgaaaag
2941 aagattgata atactcaagc catgaagaaa tattttgaaa gtgtcgatcg attcctatac
3001 tcgtgttgt gatattcagt tgccacgtac ataatggaa tcaaggatcg tcacagtat
3061 aatctgatgc tcactgaaga tgaaaaatat gtccacattt atttcggtca cattttggaa
3121 cacgaaaga ccaaacttgg gatccagcga gatcgtaac cgtttattct aaccgaacac
3181 tttatgacag tgattcgatc ggtaaatct gtggatggaa attcgcatga gctacaaaaaa
3241 ttcaaaacgt tatgcgtcga agcctacgaa gtaatgtgga ataatcgaga tttgttcgtt
3301 tcctgttca ctttgatgct cggaatggag ttgcctgagc tgtcgacgaa agcggatttg
3361 gatcatttga agaaaaccct cttctgcaat ggagaaagca aagaagaagc gagaagttt
3421 ttccacgcag tctacgaaga agccttcaat ggatcatggt ctacaaaaac gaattggctc
3481 ttccacgcag tcaaacacta ctga

Fig. 15 (sheet 2 of 2)

00000000000000000000000000000000

1 RKPWSSRSDC WTRTELRRIS QMHVNILHPQ LQTMVEQWQM RERPSLEHEN GKGSLLLNE
61 GVADIITMCP FGEVISVVFP WFLANVRTSL EIKLSDFKHQ LFELIAPMKW GTYSVKPQDY
121 VFRQLNNFGE IEVIFNDQP LSKLELHGTF PMLFLYQPDG INRDKELMSD ISHCLGYSLD
181 KLEESLDEEL RQFRASLWAR TKKTCLTRGL EGTSHYAFPE EQYLCVGESC PKDLESKVKA
241 AKLSYQMFWR KRKAEINGVC EKMMKIQIEF NPNETPKSLL HTFLYEMRKL DVYDTDDPAD
301 EGWFLQLLAGR TTFVTNPDVK LTSYDGVRSE LESYRCPGFV VRRQSLVLKD YCRPKPLYEP
361 HYVRAHERKL ALDVLSVSID STPKQSNSD MVMTDFRPTA SLKQVSLWDL DANLMIRPVN
421 ISGFDFPADV DMYVRIEFSV YVGTLTLASK STTKVNAQFA KWNKEMYTFD LYMKDMPPSA
481 VLSIRVLYGK VKLKSEEFEV GWVNMSLTDW RDELRQQFL FHLWAPEPTA NRSRIGENGA
541 RIGTNAAVTI EIISYYGGRVR MPSQGQYTYL VKHRSTWTET LNIMGDYES CIRDPGYKKL
601 QMLVKKHESG IVLEEDEQRH VWMWRRYIQQ QEPDILLIVLS ELAFVWTDRE NFSELYVMLE
661 KWKPSPVAAA LTLLGKRCTD RVIRKFAVEK LNEQLSPVTF HLFLPLIQA LKYEPRAQSE
721 VGMMALLTRAL CDYRIGHRLF WLLRAEIARL RDCDLKSEYY RRISLLMEAY LRGNEEHIKI
781 ITRQVDMVDE LTRISTLVKG MPKDVTAMKL RDELRSISHK MENMDSPPLDP VYKLGEMIID
841 KAIVLGSAKR PLMLHWKNKN PKSDLHLPFC AMIFKNGDDL RQDMLVLQVL EVMDNIWKA
901 NIDCCINPYA VLPMGEMIGI IEVVPNCKTI FEIQVGTGFM NTAVRSIDPS FMNKWIRKQC
961 GIEDEKKKSK KDSTKNPIEK KIDNTQAMKK YFESVDRFLY SCVGYSVATY IMGIKDRHSD
1021 NLMLTEDGKY VHIDFGHILG HGKTKLGIQR DRQPFILTEH FMTVIRSGKS VDGNSHELQK
1081 FKTLCEAYE VMWNNRDLFV SLFTLMLGME LPELSTKADL DHLKKTLCNF GESKEEARKF
1141 FAGIYEEAFN GSWSTKTNWL FAHKHY

Fig. 16

CONVERGENT TGF- β AND INSULIN SIGNALING
ACTIVATE GLUCOSE-BASED METABOLISM GENES

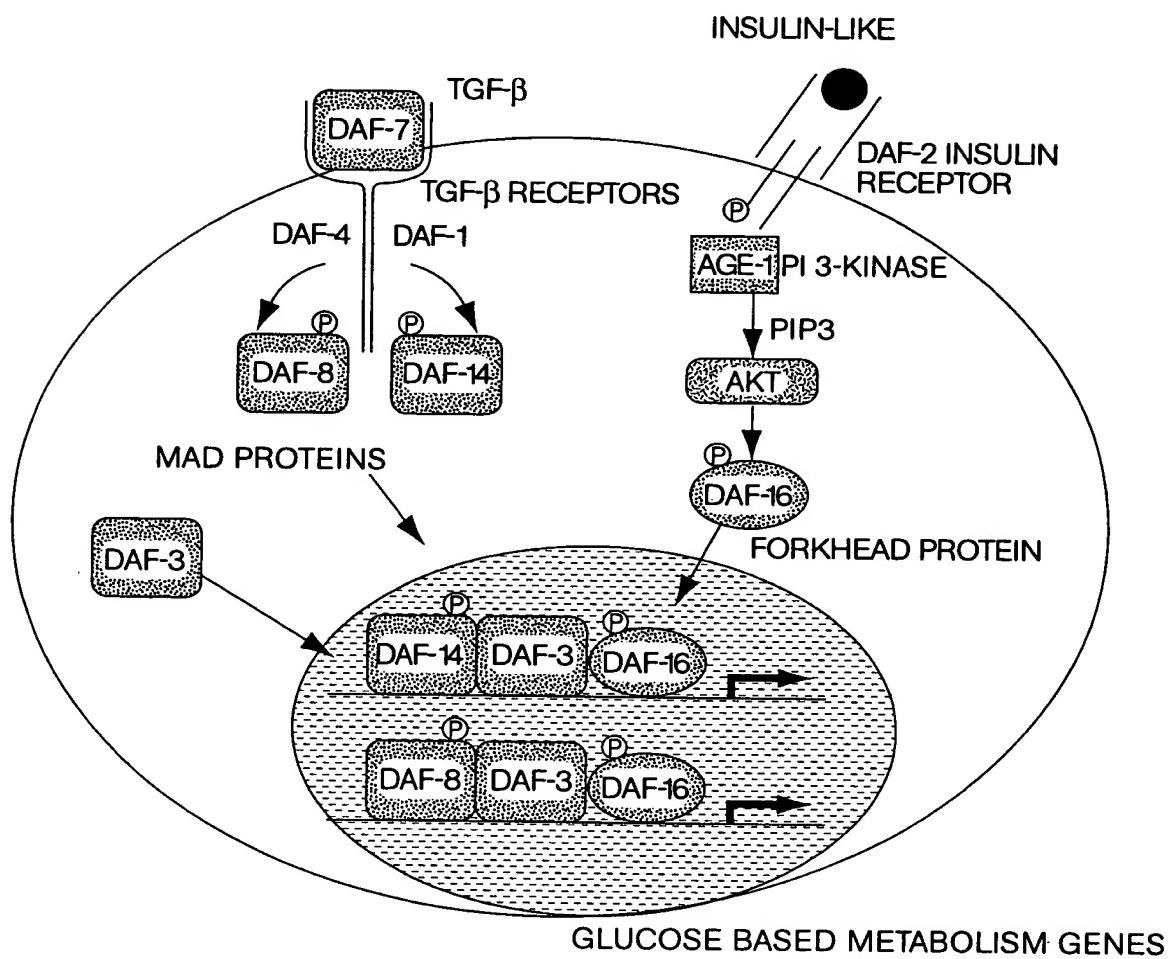


Fig. 17

**IN PHEROMONE, NO TGF β OR INSULIN-LIKE SIGNALS
CAUSES REPRESSION OF ANABOLIC GENES**

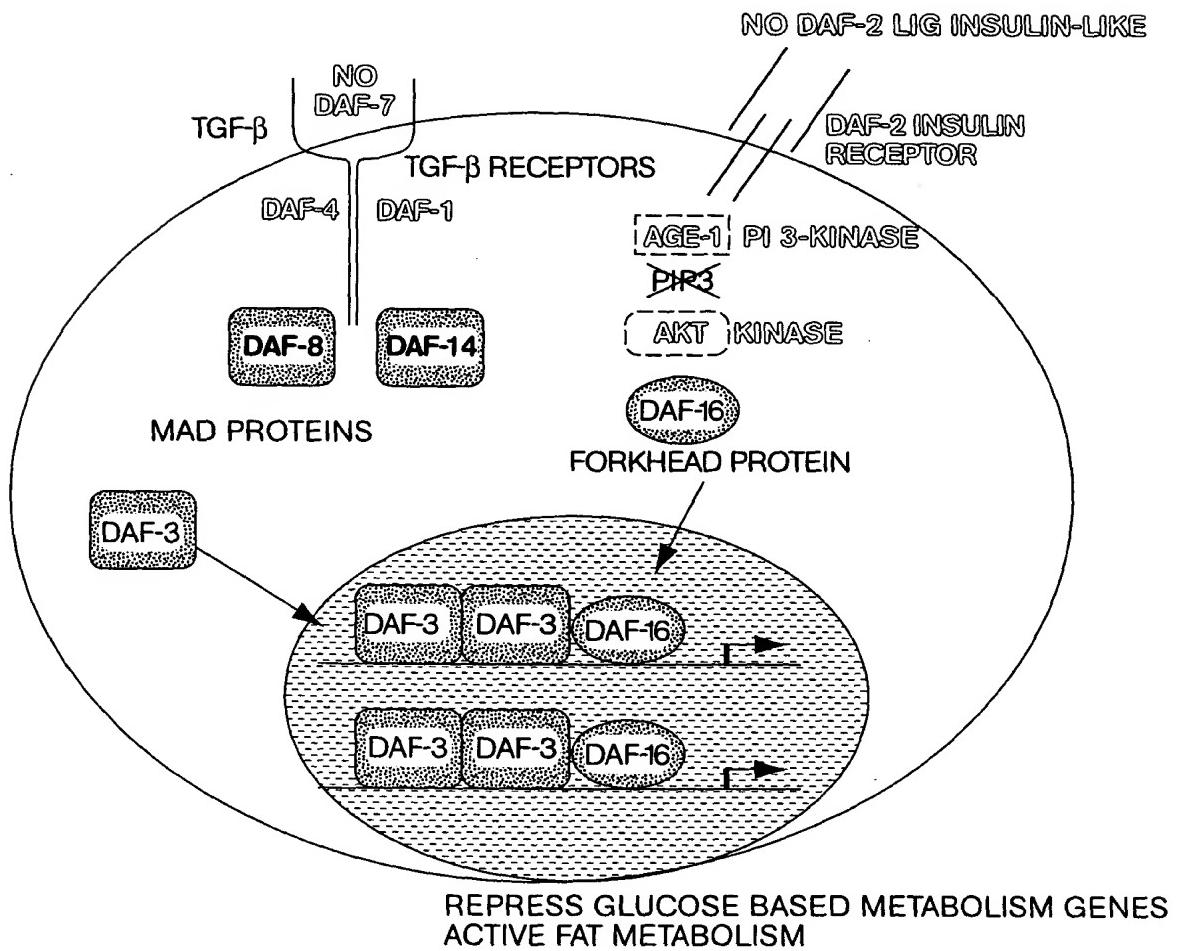
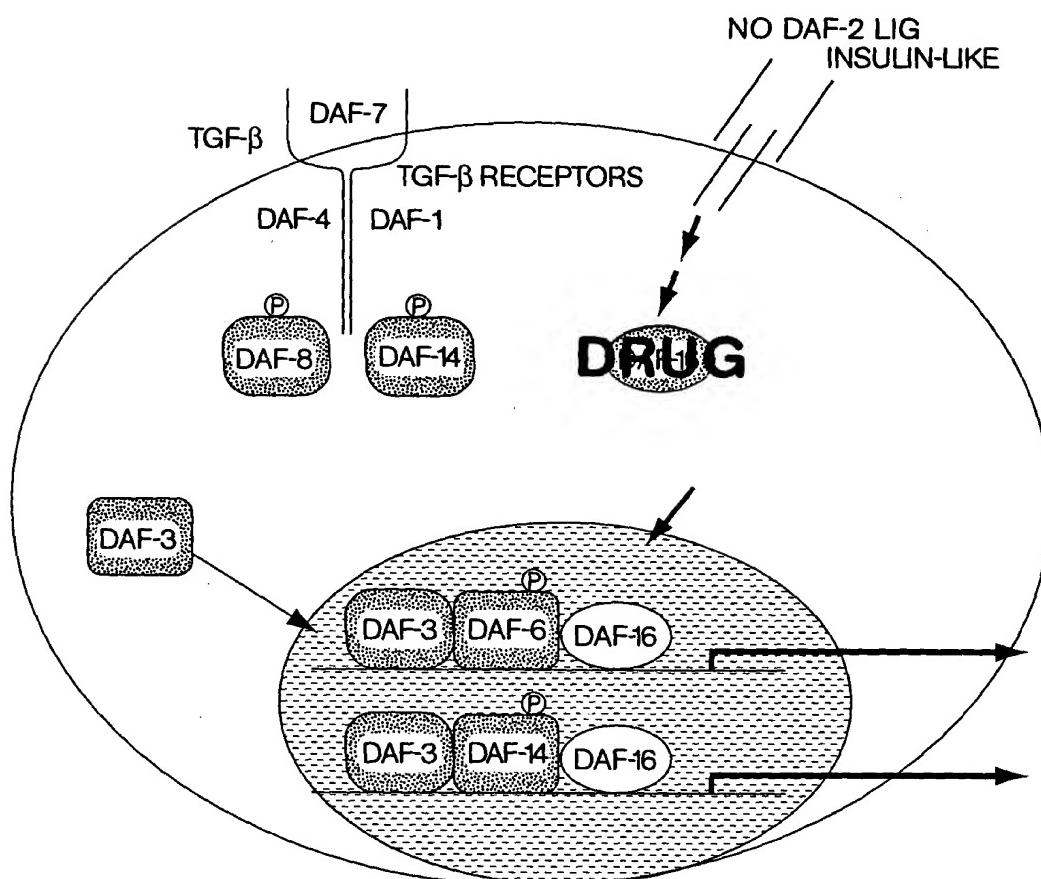


Fig. 18

DRUGS THAT INHIBIT DAF-16 OR DAF-3
 (OR PROTEINS IN THE PATHWAY)
 CAN BE DISCOVERED USING REPORTER GENES
 BEARING THEIR COGNATE BINDING SITES



DRUG CAUSES A DECREASE IN DAF-16 ACTIVITY, ACTIVATING
 THE REPORTER GENE LIKE A DAF-16 MUTANT.
 THIS BYPASSES THE NEED FOR INSULIN

Fig. 19

DRUGS THAT INHIBIT DAF-3 WILL CURE
THE DIABETES CAUSED BY A LACK OF DAF-7

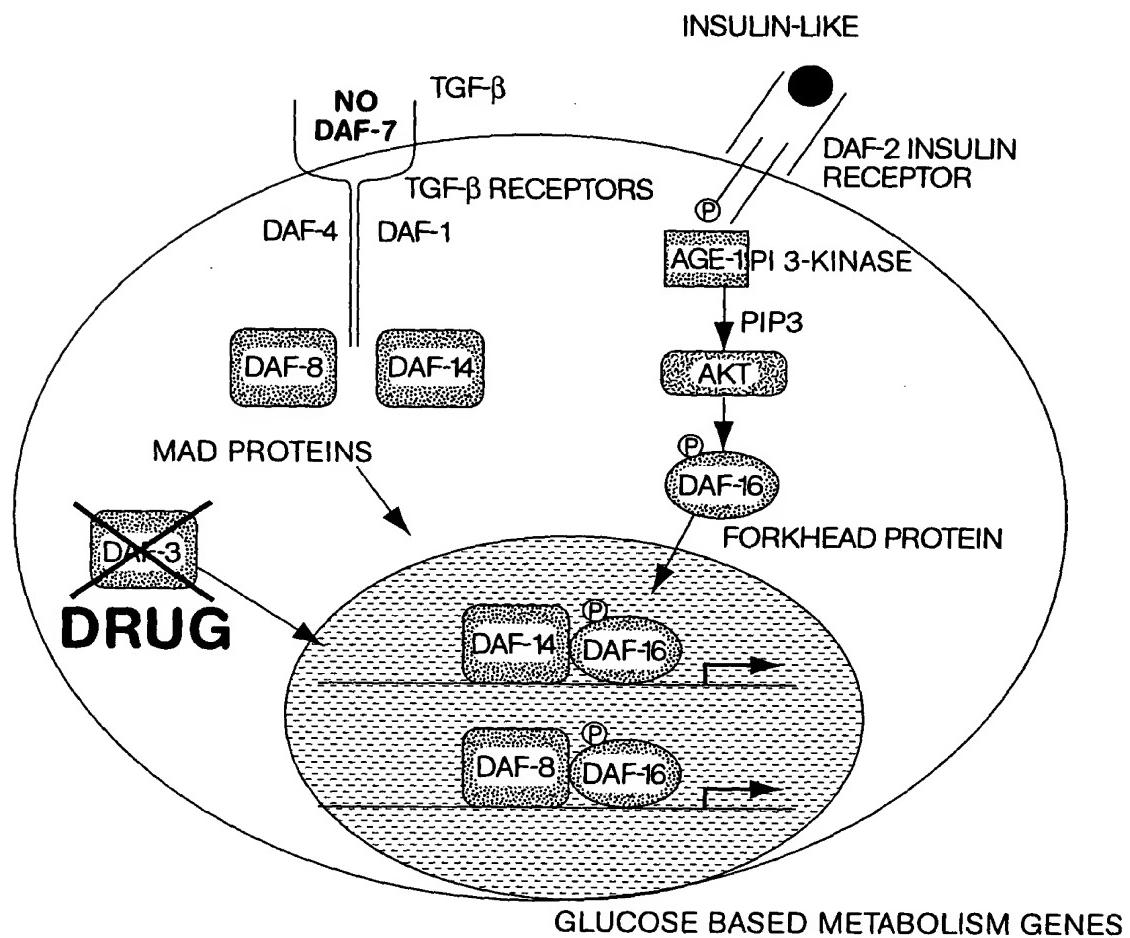


Fig. 20

四庫全書

Fig. 21A (sheet 1 of 3)

Hnf3a	SLITMAIORA SLITMAIOQA ELITTAIWAS DIIAKALESA EISQAIESA DLITKAIESS	PSKWLTLSEI PCKVLTLESEI PEKRLTLAQEI PDGRILKEENEI PEKRLTLAQEI AEKRLTLSQI	YOWIMDLFPPY YOWIMDLFPPY YEWMVQNVPY YQWESDNIPY YEWMVRTVPY YEWMVKSVPY	YRQONQQR... YRDNQQR... FRDKGDSNNS FRDKGDSPEEA FRDKGDSNNS FRDKGDSNNS	WONSIRHS WONSIRHS AGWKNSIRHN AGWKNSIRHN AGWKNSIRHN AGWKNSIRHN	LSEND LSEND LSIHS LSIHS LSIHS LSIHS
Hnf3g	D16123a467891011 D1612567891011	Afx	-LIT-AI--A	P-KRLTL--I Y-W--PY F-D--		
Fkhr						
Consensus						
Hnf3a	CFVKVARSPD CFVKVARSPD	KPGKGSWTE KPGKGSWAE	HPDSC HPSSG	NM NM	FENGCYLRRQ FENGCYLRRQ	KRFKC KRFKL
Hnf3g	REMRION REMRION	GAGKSSWWV GAGKSSWWV	NPD NPD	PRTRERSNT PRTRERSNT	IETTTKAOLE IETTTKAOLE	KSRRG KSRRG
D16123a467891011	D1612567891011	Afx			MDSSSKLJRG MDNNNSKFAKS	RSKAP RSRAA
Fkhr						271
Consensus	-F--V-N--E	--GKSSWW-L	NP--GK-G-- PRR--R-N--K--	--KS--		385
Hnf3a	EKOPGAG... EEKVKG...	GGGSGGGGS GSGASTTRNC	GAKGGPESRK TGSAASTTP	DPSGASNPSA AATVTSP	DSPLHRGVHG KTGQL	321 213
Hnf3g	AKKRICKERAL AKKRICKERAL	MGSTHSTLNG MGSTHSTLNG	NSIAGSIQTI NSIAGSIQTI	SHDLYDDSM SHDLYDDSM	QCAFDNVPSS QCAFDNVPSS	257 257
D16123a467891011	D1612567891011	Afx	KKKP... KKKA... -KK--	.SVTPAPPEC .S.LQSQQEC	ATPTSPVGHF AG.DSPGQF SKWPASEPGSH	FRPT FRPT FRPT
Fkhr				--E--L--G-- --E--S--G-- --E--S--G--		312 382 208
Consensus						271
Hnf3a	EGAPAPGPAA .OPPPPAPEP	SPOTLDHSGA EAQGGEDEVGA	TATGGASELK IDCGS...	TASSSTAPP TASSTP	SSCPGALASV PAISHP	376 248
Hnf3g	QSNLSD... QSNLSD... -SN-S-- - -E-SS-- - 495
D16123a467891011	D1612567891011	Afx				
Fkhr						
Consensus						
Hnf3a	AHGLAPHESO Hnf3g	LHLKGDPHYS YFTGHELP	FNHFFSINNL GDLKLDAPYN	MSS.SEQQHK MSEQTPAPPK	LDFKAYEQAL LD...	QYSPY GFGGX
Hnf3g	D16123a467891011 D1612567891011	.DIYDDEEF. .DIYDDEEF.	PSWVGESV PSWVGESV	PAIP... PAIP...	V ..
Afx	E.LLDGENLT	SSHSSLRSRG	LSG... SSPTSLTVST	... QSSEGTWMQO	... TPCYSFAPPN	351 476 337 426
Fkhr	ENLLDNLL	-D-TE--	-S--E--	-E--S--	-	-Y
Consensus						550

Fig. 21A (sheet 2 of 3)

Hnf3a	GSTLPASLPL	GSASVTRSP	IEPGSALEPAY	YOGVYSRPPV	NTS	473
Hnf3g	GAE	GGEPGVY	GGEPGVY	GGLYSRSL	NAS	347
D16123a467891011	SDIVD	RTDQMRIDAT	THIGGV0	IKOESKPIK	HEPIAAPPY	HELN5
D1612567891011	SDIVD	RTDQMRIDAT	THIGGV0	IKOESKPIK	HEPIAAPPY	HELN5
Afx	SSSLFSP	AE	GPLEAGEGCCF	SSSOALEAL	ESDTTPPPAD	VLMTO
Fkhr	GQSSMSPLPQ	MPIQLQDNK	SSYGGMSQYN	CAPGLLKELE	ESDSPEH	479
Consensus	S	E	E	E	E	605
Hnf3a						
Hnf3g						
D16123a467891011	YRGSCAO NP	LTERNPIVPS	TNFKPMPPLPG	AYGNYQNGGI	TPINWLSTS N	SSPLP
D1612567891011	YRGSCAO NP	LTERNPIVPS	TNFKPMPPLPG	AYGNYQNGGI	TPINWLSTS N	SSPLP
Afx	YDPILSOAPT	LL	LL	LLGG	SKLA	PKPLE
Fkhr	VDPGVAOPNS	RVIGQNVMMG	PNSVMSTYGS	QASH	NKMM	NPSHTHPGH
Consensus	V	Q	E	E	E	660
Hnf3a						
Hnf3g						
D16123a467891011	GIQS CGIVAA	QHTVASS SAL	PIDLENLTLP	DQPLMDTM	473
D1612567891011	GIQS CGIVAA	QHTVASS SAL	PIDLENLTLP	DQPLMDTM	347
Afx	ARGPSSLVPT	LSMIA APPVM	AS	APIPKALGT	PVLTPPTEAA	S
Fkhr	AVNGRPLPH	VSTM PHTSGM	NRLTQVKTPV	QVPLPHPMQM	SALGGYSSVS	SCNGY
Consensus	-	-	-	E	-	715
Hnf3a						
Hnf3g						
D16123a467891011	DVDA	LIRH ELSQAG	GQH IHEDL
D1612567891011	DVDA	LIRH ELSQAG	GQH IHEDL
Afx	QDR	MPO DLD MY	MEN LECDMDN	GLDFN FEPDP	501
Fkhr	GRM GLLHQEK	LP SLD L.GMF	IER LD CDMES	IRNDLMDGD	PNOSF	641
Consensus	-	-	D	E	-	770
Hnf3a						
Hnf3g						
D16123a467891011	473
D1612567891011	347
Afx	510
Fkhr	PHSVKTTTTS	WVSG	WVSG	WVSG	WVSG	784
Consensus	-	-	-	-	-	

Fig. 21A (sheet 3 of 3)

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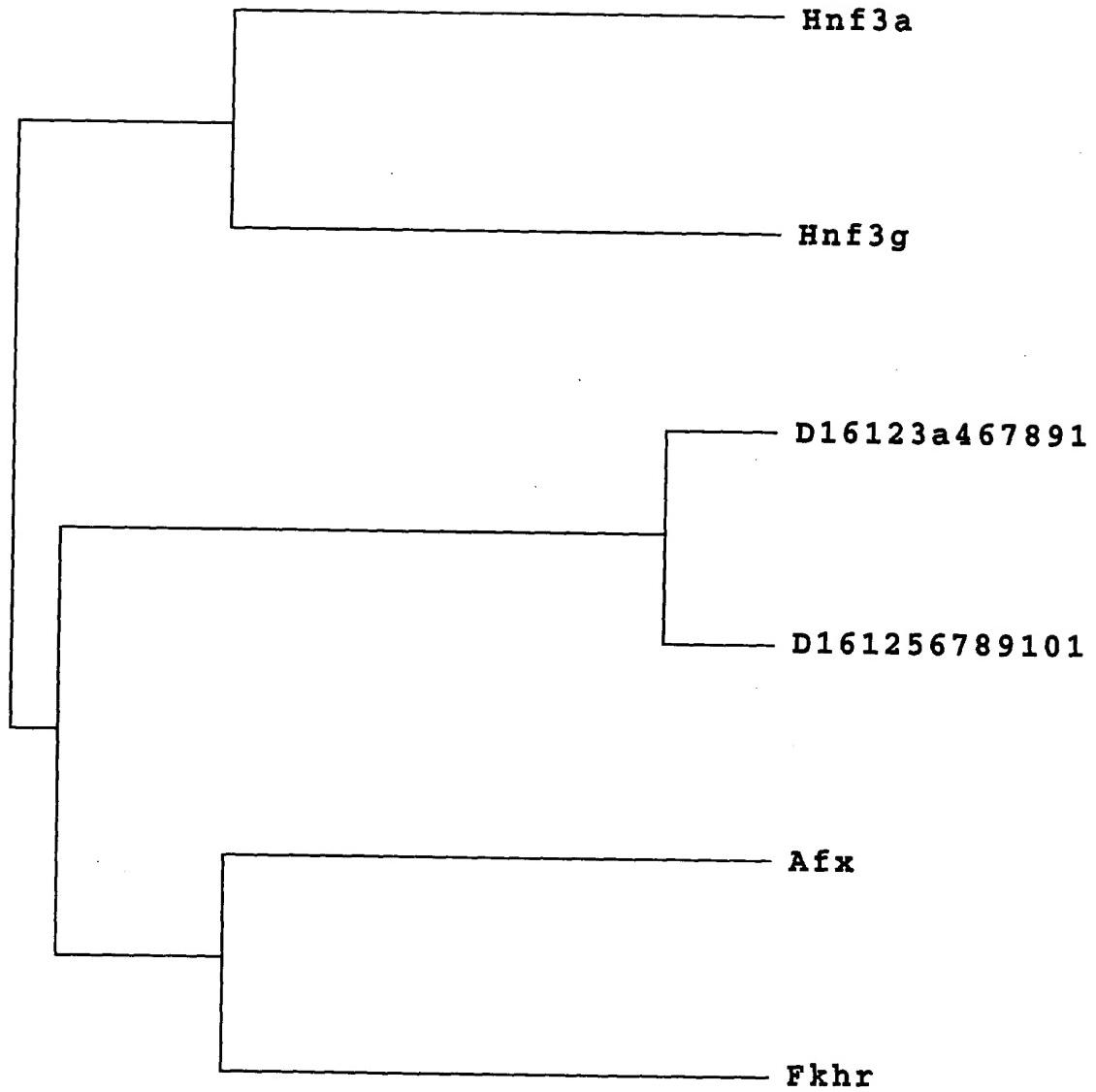


Fig. 21B

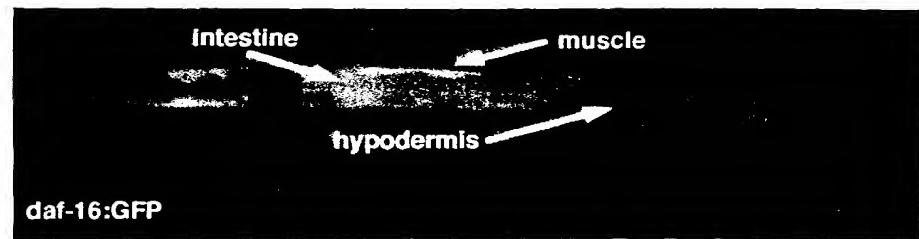


Fig. 22

INJECTION OF DAF-7 BYPASSES OBESITY-INDUCED DEFECTS IN INSULIN-REGULATION OF METABOLISM

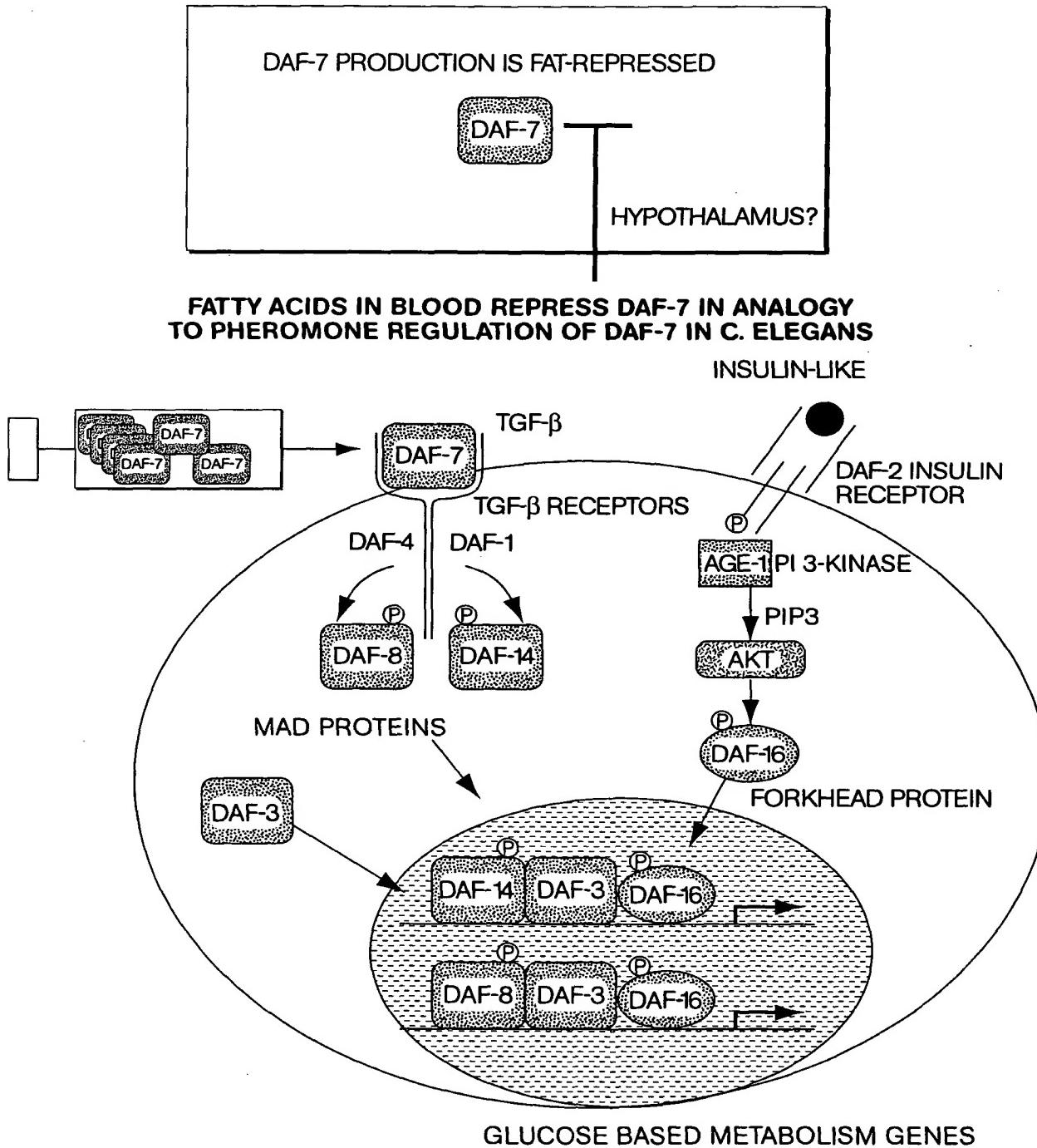


Fig. 23

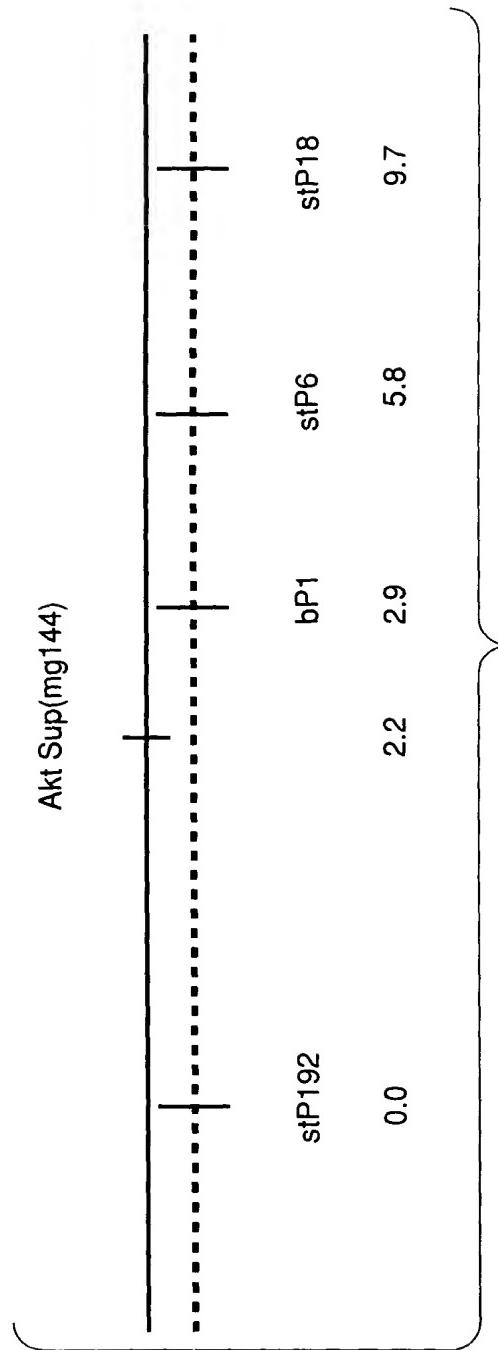


Fig. 24

Comparison of the human AKT protein sequence to the cosmid sequence C12D8, located in the genetic interval where sup(mg144) maps. Numbering in the AKT protein sequence by amino acid residues, and in the cosmid sequence by nucleotide position.

Score = 450 (207.4 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 79/121 (65%), Positives = 97/121 (80%), Frame = +1

Query: 319 EVLEDNDYGRAVDWWGLGVV ру EMCGRLPFYNQDHEKLFELILMEEIRFPRTLGPEAKS 378
+VL+D+DYGR VDWWG+GVV ру EMCGRLPFY++DH KLFELI+ ++RFP L EA++
Sbjct: 33685 QVLDDHDYGRСVДWWGVGVV ру EMCGRLPFYSKDHNKLFELIMAGDLRFP SKLSQEART 33864

Query: 379 LLGGLLKKDPТQRLGGGSEDAKEIMQHРFFFANIVWQDVYEKKLSPPFKPQVTSETDTRYFD 439
LL+GLL KDPTQRLGGG EDA EI + FF + W+ Y K++ PP+KP V SETDT YFD
Sbjct: 33865 LLTGLLVKDPTQRLGGGPEDALEICRADFFRTVDWEATYRKEIEPPYKPNVQSETDTSYFD 34047

Score = 256 (118.0 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 48/66 (72%), Positives = 59/66 (89%), Frame = +1

Query: 146 TMNEFEYLKLLGKGTFGKVILVKEATGRYYAMKILKKEVIVAKDEVAHTLTENRVLQNS 205
TM +F++LK+LGKGTFGKVIL KEK T + YA+KILKK+VI+A++EVAHTLTENRVLQ
Sbjct: 32314 TMEDFDFLKVLGKGTFGKVILCKEKTQKLYAIKILKKDVIAREEVАHTLTENRVLQRC 32493

Query: 206 RHPFLT 211
+HPFLT
Sbjct: 32494 KHPFLT 32511

Score = 190 (87.6 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 36/45 (80%), Positives = 37/45 (82%), Frame = +2

Query: 276 KLENLMLDKDGHIKITDFGLCKEGIKDGATMKTFCGTPEYLAPEV 320
KLENL+LDKGDHIKI DFGLCKE I G TFCGTPEYLAPEV
Sbjct: 33509 KLENLLDKDGHIKIADFGLCKEEISFGDKTSTFCGTPEYLAPEV 33643

Score = 188 (86.7 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 37/57 (64%), Positives = 42/57 (73%), Frame = +3

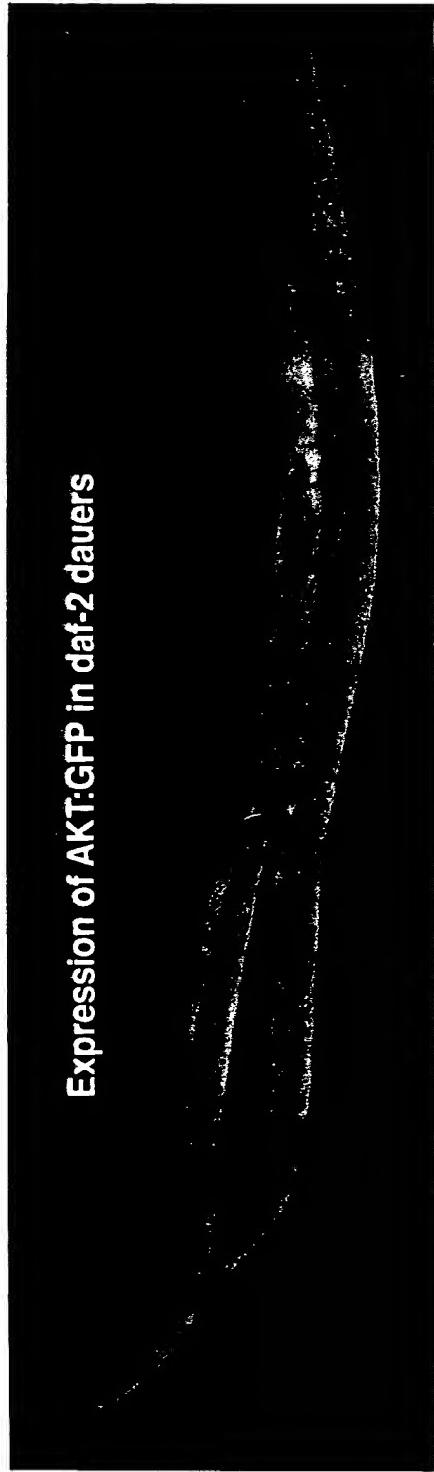
Query: 209 FLTALKYSFQTHDRLCFVMEYANGGELFFHLSRERVFSEDRARFYGAЕIVSALDYLH 265
+ LKYSFQ LCFVМ++ANGGELF H+ + FSE RARFYGAЕIV AL YLH
Sbjct: 32667 YFQELKYSFQEHQHLCFVMQFANGGELFTHVRKCGTFSEPRARFYGAЕIVLALGYLH 32837

Score = 166 (76.5 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 29/59 (49%), Positives = 42/59 (71%), Frame = +1

Query: 53 NNFСVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHВETPEEREЕWATAIQTVADGLK 111
+ F++ Q M E+PRPN F++RCLQWTTVIERTF+ E+ E R+ W AI++++ K
Sbjct: 31846 STFAIFYFQTMLFEKPRPNFMVRCLQWTTVIERTFYAESAEVRQRWIHAIESISKYK 32022

Score = 134 (61.8 bits), Expect = 5.2e-167, Sum P(8) = 5.2e-167
Identities = 24/33 (72%), Positives = 30/33 (90%), Frame = +3

Query: 210 LTALKYSFQTHDRLCFVMEYANGGELFFHLSRE 242
L LKYSFQT+DRLCFVME+A GG+L++HL+RE
Sbjct: 33156 LQELKYSFQTNDRLCFVMEFAIGGDLYYHLNRE 33254



Expression of AKT::GFP in *daf-2* dauers

Fig. 26A

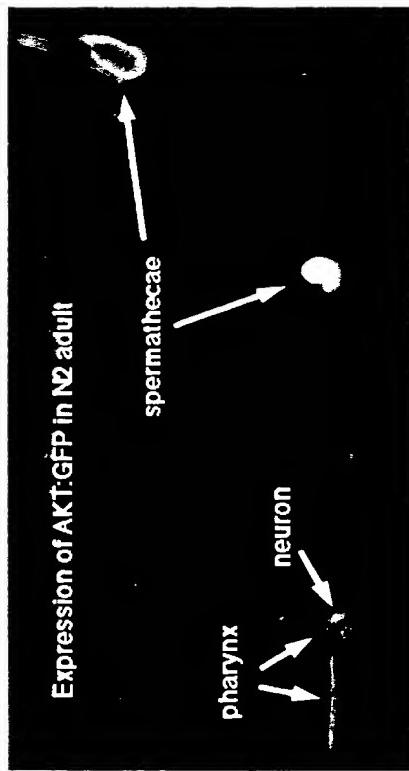


Fig. 26B

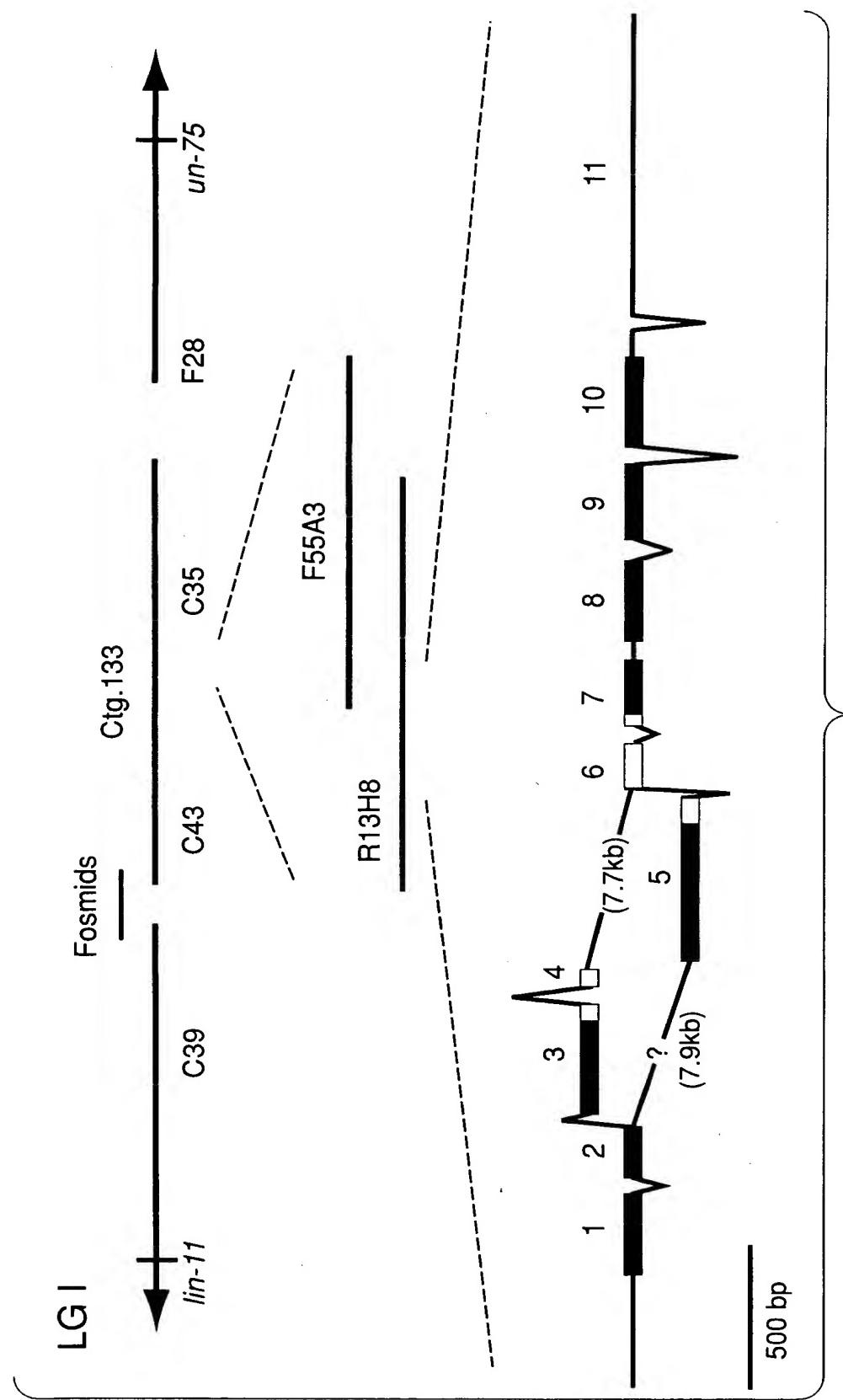


Fig. 27